Familial 'hashitoxic' periodic paralysis[1]

Alexander K C Leung MCRP(UK) FRCP(C)
Faculty of Medicine, University of Calgary Foothills Hospital, 1403–29th Street NW, Calgary, Alberta, Canada

Summary: Four members of a Chinese family who had thyrotoxicosis and periodic paralysis are described. Two of these patients had 'hashitoxicosis' (Graves' disease and Hashimoto's thyroiditis) as evidenced by the presence of thyroid antibodies in addition to elevated thyroxine (T4) levels. The other two patients were not available for testing. The association of the familial occurrence of 'hashitoxicosis' and periodic paralysis does not appear to have been reported previously.

Introduction

Periodic paralysis is a rare myopathic disorder characterized by episodic attacks of symmetrical flaccid paralysis typically precipitated by exposure to cold, heavy carbohydrate meals, rest after exercise, alcohol, infection, accidental trauma, menstruation, or emotional excitement (Feldman & Goldberg 1969). The serum potassium level may be normal, low or high during paralytic attacks (Fisher 1982). Although usually familial (Melnick *et al.* 1983), sporadic cases may occur often in association with hyperthyroidism (Papouchado 1980). The latter is most frequently seen in the Oriental population (Papouchado 1980, McFadzean & Yeung 1967). McFadzean & Yeung (1967) reported 25 cases of thyrotoxic periodic paralysis among 1366 Chinese patients with thyrotoxicosis. In none was there a family history. The purpose of this paper is to report the familial occurrence of periodic paralysis in patients with 'hashitoxicosis' (Graves' disease and Hashimoto's thyroiditis). The association, to my knowledge, has not previously been reported.

Case reports

Case 1: A 33-year-old Chinese air-conditioning mechanic presented with classical symptoms and signs of thyrotoxicosis in June 1980. This was manifested by nervousness, irritability, heat intolerance, weight loss of 9 kg in six months despite an increased appetite, exophthalmos, tremor of hands, tachycardia and a diffuse toxic goitre. Laboratory investigations at that time revealed a thyroxine (T4) of 23.7 μg/dl (normal 5–12), triiodothyronine (T3) of 800 ng/dl (normal 70–230), T_3 resin uptake of 51.8% (normal 25–35), free thyroxine index (T7) of 12.3 (normal 1.25–4.55) and thyrotropin simulating hormone (TSH) of 2.6 μU/ml (normal up to 5). He was started on propylthiouracil 50 mg three times daily.

In May 1981, he had several episodes of periodic paralysis. Usually this occurred in the evening after a day's work, a heavy carbohydrate meal, a cold drink followed by a rest. Although remaining awake, he was not able to move his body. This usually lasted for several hours. On examination, he was slightly hyperthyroid with a resting pulse of 90/minute and a thyroid gland $1\frac{1}{2}$ times the normal size. Thyroid function tests were as follows: T4 15.8 ug/dl, T3 454 ng/dl, T3 uptake 46.8%, T7 7.39 and TSH 0.5 μU/ml. Thyroid thyroglobulin and microsomal antibodies were positive to a titre of 1:100 and 1:1600 respectively. Serum potassium was 3.6 mmol/l, sodium 142 mmol/l and chloride 105 mmol/l. The dosage of propylthiouracil was increased to 100 mg three times daily, and in October 1981 he was clinically and biochemically euthyroid on this medication. The episodes of periodic paralysis ceased.

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Case 2: The 25-year-old brother of Case 1 presented in December 1978 with a two-month history of irritability, insomnia, frequent bowel movements, tremor of hands, weight loss of 3 kg despite an increased appetite, and periodic paralysis. The paralysis usually occurred in the morning, after a heavy meal, exposure to cold, and exertion on the day before. All the attacks lasted for less than half an hour. On examination, he was hyperthyroid with lid retraction, lid lag, tachycardia, wide pulse pressure, hand tremor and a diffuse goitre which was four times normal size. Thyroid microsomal antibodies were positive to a titre of 1:1600. The serum potassium was 4.1 mmol/l, sodium 143 mmol/l and chloride 105 mmol/l. He was treated with propylthiouracil for 6 months. He had a relapse in September 1981 and was treated with propylthiouracil for one year.

Case 3: The 25-year-old sister of Cases 1 and 2 had thyrotoxic symptoms and periodic paralysis at the age of 15. According to her brother, she was treated with antithyroid medication. She is now in Australia and not available for testing.

Case 4: The 54-year-old mother of Cases 1, 2 and 3 had thyrotoxicosis and periodic paralysis at the age of 50. She was treated with antithyroid medication for 9 months. She is in Hong Kong and not available for testing.

Discussion

Hyperthyroidism can be associated with myasthenia gravis, thyrotoxic myopathy, exophthalmic ophthalmoplegia and periodic paralysis (Ali & Akavaram 1980). Although periodic paralysis was first described by Hartwig in 1874 (Johnson & Winternitz 1984), its association with hyperthyroidism was not known until Rosenfeld (1902) reported the first case. Subsequently, Dunlap & Kepler (1931) described 4 more cases of periodic paralysis in association with hyperthyroidism.

Shah *et al.* (1979) reported a Caucasian female whose father and uncle had familial hypokalaemic periodic paralysis and who developed thyrotoxic periodic paralysis at the age of 24. At present it is not clear whether hyperthyroidism merely triggers an otherwise latent periodic paralysis, or whether thyrotoxic periodic paralysis can be differentiated as a distinct entity. If the manifestations of thyrotoxicosis are excluded, the clinical pictures are indistinguishable from those of idiopathic familial hypokalaemic periodic paralysis. In both forms, the serum potassium level is usually decreased, but not always below normal range, during attacks (Ali & Akavaram 1980). However, patients with thyrotoxic periodic paralysis tend to be older at the time of presentation, usually in the third, fourth and fifth decades, in contrast to the first two decades in patients with familial periodic paralysis. Although there is a preponderance of males in both forms, the male:female ratio is 3:1 in familial periodic paralysis and 20.5:1 in thyrotoxic periodic paralysis (Jackman & Jones 1964). In thyrotoxic periodic paralysis but not in familial periodic paralysis, the attacks became more severe on thyroid administration (Kusakable *et al.* 1976) and were alleviated by propranolol administration (Yeung & Tse 1974).

It is possible that excessive amounts of thyroid hormone induce an increase in the permeability of the muscle membrane to electrolytes, with resulting influx of potassium into the cells. This is supported by the fact that the attacks cease when the hyperthyroidism has been treated successfully but may recur if hyperthyroidism escapes control. Also, periodic paralysis has been reported to be associated with transient hyperthyroidism (Leung 1984). It is possible that thyroid antibodies may potentiate this effect. Thyrotoxic periodic paralysis, although usually considered to be sporadic, may be familial if the affected members have thyroid antibodies. The cases described in this paper suggest that the incidence of thyrotoxic periodic paralysis tends to be higher in patients with 'hashitoxicosis'.

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